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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,114	07/18/2003	Yerramilli V.S.N. Murthy	051091-2001	4452

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1617	

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10/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/623,114	MURTHY ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/27/2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-48* is/are pending in the application.

4a) Of the above claim(s) *38-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 27, 2007 has been entered.

It is noted that claims 38-48 drawn to a method of treating a bacterial infection is withdrawn from consideration because they are non-elected invention. Accordingly, claims 25-37 are being examined.

Action Summary

The rejection of claims 25-31 under 35 U.S.C. 103(a) as being unpatentable over Camaggi et al. (U.S.Patent No. 5,336,664) of record in view of Nagy (U.S.Patent No. 4,872,411) is hereby expressly withdrawn in view of Applicants' amendment.

The rejection of claims 32-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Camaggi et al. (U.S.Patent No. 5,336,664) of record in view of Nagy (U.S.Patent No. 4,872,411) and further in view of Highsmith et al. (U.S.Patent No. 2002/0065198 A1) is hereby expressly withdrawn in view of Applicants' amendment.

The rejection of claims 34-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shuster et al. (US 2004/0198704 A1) is hereby expressly withdrawn in view of new grounds of rejection.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 25-35 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nagabhushan (U.S.Patent No. 4,311,857) of record in view of Bundgaard (1985).

Nagabhushan teaches a pharmaceutical composition comprising D-(threo)-1-p-methylsulfonylphenyl-2-chloroacetamido-3-fluoro-1-propanol (also known as **florfenicol**) together with a compatible pharmaceutically acceptable carrier. (column 10, lines 5-10, column 20 lines 10-11). Nagabhushan demonstrates that above composition can be formulated in an injectable solution with concentration of 250mg/ml of florfenicol as an active drug. (column 11, lines 20-31, column 12, lines 55-61, Formulation 5). Nagabhushan teaches that the ester derivatives of florfenicol including formic, acetic, propionic, triemthylacetic, **butyric**, isobutyric and valeric etc., are also

antibacterially active as florfenicol. (column 4 lines 22-60). Nagabhushan teaches that the composition can be formulated to be administered parenterally via intramuscular injection and that the dosage to be administered depends on the stage and severity of the injection, the susceptibility of the infecting organism to the antibacterial and the individual characteristics of the animal species being treated. (column 10, lines 55-66). Nagabhushan teaches that **propylene glycol** is compatible with florfenicol. (column 11, lines 5-20, formulations).

Nagabhushan does not expressly teaches combinations of florfenicol esters in a single formulation and the specific concentration of florfenicol.

Bundgaard teaches that ester formation has long been recognized as an effective means of increasing the aqueous solubility of drugs containing a hydroxyl group, with the aim of developing prodrug preparation suitable for parenteral administration. (page 7, last sentence). Bundgaard teaches that esters convert rapidly in vivo to the active parent drug by hydrolysis. (page 8, second paragraph).

It would have been obvious to one of ordinary skill in the art to employ ester derivatives of florfenicol including florfenicol butyrate, florfenicol propionate and florfenicol acetate etc.. taught by Nagabhushan in a single formulation for parenteral administration because ester prodrugs taught by Nagabhushan have beneficial effect in parenteral formulation because of they increase the aqueous solubility of drugs containing a hydroxyl group such as florfenicol and this is well known and recognized effective means of preparing parenteral formulation as taught by Bundgaard. One would have been motivated to make such a modification in order to achieve the active

florfenicol in vivo rapidly by hydrolysis of prodrug of florfenicol ester taught by Nagabhushan. Further, to employ more than one active esters of florfenicol in a single formulation is obvious because each of the esters of florfenicol have antibacterial activity as taught by Nagabhushan. The motivation for combining the components flows from their individually known common utility (see In re Kerkhoven, 205 USPQ 1069(CCPPA 1980)). With regard to the property of the composition forms a drug depot when injected into a mammal is obvious because the obvious composition taught by Nagabhushan as modified by Bundgaard constitutes with the same active agents cannot have mutually exclusive properties. Further, the specific concentration of florfenicol set forth in the claim is obvious because Nagabhushan demonstrates injectable composition of active agent in concentration of 250mg/ml and that the dosage to be administered depends on the stage and severity of the injection, the susceptibility of the infecting organism to the antibacterial and the individual characteristics of the animal species being treated. Therefore, one of ordinary skill in the art would have been motivate to optimize the concentrations of the parenteral formulation of Nagabhushan as modified by Bundgaard for the specific individuals being treated as determined by their diagnosis and the progress in their condition.

Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nagabhushan (U.S.Patent No. 4,311,857) of record in view of Bundgaard (1985) as applied to claims 25-35 above, and further in view of Shuster et al. (US 2004/0198704 A1) of record.

Teachings of Nagabhushan and Bundgaard as applied as before. Neither Nagabhushan nor Bundgaard teach the glycerol formal.

Shuster et al. teach novel formulation comprising a compound having structural formula I of florfenicol and its **ester derivatives** e.g. 1-hydrocarboncaroxylates of the formula I wherein Z is an **acyl group of a hydrocarboncarboxylic acid** having **up to 16 carbon atoms** that may be saturated, unsaturated, straight chain or **branched chain**. (pages 2-4, [0019], [0027], [0047], [0048], [0049]) This formula encompasses Applicant's florfenicol butyrate recited in claim 34. Shuster et al. teach the composition can be formulated with pyrrolidone solvents such as **N-methyl-2-pyrrolidone** and 2-pyrrolidone or **glycerol formal** or **propylene glycol**, **polyethylene glycol**, ethanol and DMSO. (page 6 [0077]). Shuster et al. teach that the formulation is useful for treating bacterial infection of cattle and other animals. (page 2 [0016]). Shuster et al. teach that the formulation can be administered by **injection**. ([0075]). Shuster et al. teach that the precise dose to be administered depend on the stage and severity of the infection and the individual characteristics of the **animal** species being treated, as will be appreciated by the one of ordinary skill in the art. (page 7, [0089]).

It would have been obvious to one of ordinary skill in the art to formulate combine glycerol formal in the obvious composition of Nagabhushan as modified by Bundgaard because Shuster et al. teach that glycerol formal and propylene glycol are all compatible with florfenicol ester in injectable formulation and because Nagabhushan teaches that any compatible carriers can be employed in the ester prodrug of florfenicol in a formulation. One would have been motivated to combine glycerol formal in the obvious

composition of Nagabhushan as modified by Bundgaard in order to achieve a stable parenteral composition comprising prodrug esters of florfenicol with the compatible carriers taught by Shuster et al. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Response to Arguments

Applicants' arguments filed July 27, 2007 have been fully considered but they are not persuasive. Applicants argue that there is absolutely no disclosure in Shuster of the advantages properties of a composition comprising florfenicol butyrate and the claimed pharmaceutically acceptable solvents wherein the composition is formulated as a composition for administration to a mammal by injection. This is not found persuasive because the advantages of ester prodrugs are long recognized as an effective means of increasing the aqueous solubility of drugs containing a hydroxyl group in view of Bundgaard. Applicants argue that the superiority of florfenicol butyrate compared to NuFlor (i.e. florfenicol) is clearly supported by the specification and Applicants' Declaration submitted with the previous Office Action. Applicants argue that Example 8 and FIG 8 show that florfenicol butyrate has a better pharmacological profile than NuFlor and without the adverse reactions. The declaration have been carefully reviewed and considered. However, it is not persuasive because the comparison of NuFlor (i.e. florfenicol) versus florfenicol butyrate is noted. However, Applicants surprising and unexpected result of florfenicol butyrate (florfenicol ester prodrug) having better pharmacological profile than NuFlor is an expected result in view of Bundgaard

who teaches that ester formation has long been recognized as an effective means of increasing the aqueous solubility of drugs containing a hydroxyl group. Therefore, the employment of ester form of florfenicol results in better pharmaceutical profile is expected and well recognized in view of Bundgaard. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Kim
Primary Examiner
Art Unit 1617

Jmk
October 9, 2007